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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,474	09/06/2005	Stefan Herz	049202/286618	2299
826 7590 07/02/2008 ALSTON & BIRD LLP BANK OF AMERICA PLAZA 101 SOUTH TRYON STREET, SUITE 4000 CHARLOTTE, NC 28280-4000				
EXAMINER KUBELIK, ANNE R				
ART UNIT 1638		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/523,474

**Applicant(s)**

HERZ ET AL.

**Examiner**

Anne R. Kubelik

**Art Unit**

1638

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 January 2008 and 17 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-15, 17-20 and 23-27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 27 is/are allowed.
- 6) ☒ Claim(s) 1, 3-10, 12-15, 18-20 and 23-26 is/are rejected.
- 7) ☒ Claim(s) 2, 11 and 17 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 January 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

#### **DETAILED ACTION**

1. Claims 1-15, 17-20 and 23-27 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The objection to claim 2 because there is a plurals disagreement is withdrawn in light of Applicant's amendment of the claim.
4. The objection to claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of Applicant's amendment of the claim.

#### ***Claim Rejections - 35 USC § 112***

5. Claim 10 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 27 September 2007, as applied to claims 3, 6-8, 10, 12, 15 and 24. Applicant's arguments filed 16 January 2008 have been fully considered but they are not persuasive.

Claim 10 is indefinite in its recitation of "wherein expression of said gene of interest includes RNA trans-splicing". Recitation of "includes" makes it unclear if trans-splicing is actually involved.

Applicant urges that the MPEP indicates that "including" is synonymous with "comprising" (response pg 21).

This is not found persuasive because the phrase “wherein expression of said gene of interest comprising RNA trans-splicing” makes no sense as a limitation.

***Claim Rejections - 35 USC § 102***

6. Claims 1, 3-8, 12, 14-15, 18-20, 23-24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Herz et al (WO 02/055651). The rejection is repeated for the reasons of record as set forth in the Office action mailed 27 September 2007, as applied to claims 1, 3-8, 12, 14-15, 18-20 and 23-24. Applicant's arguments filed 16 January 2008 have been fully considered but they are not persuasive.

Herz et al disclose a method of tobacco plastid transformation comprising introducing separately into plastids two DNA constructs. The second DNA construct comprises a first region homologous to the plastid genome (trnL/ycf5) and a first sequence of interest (an promoterless aphA6 coding region operably linked to the rbcL 3' sequence) and the first DNA construct comprises a second region homologous to the plastid genome (rpl32/sprA), a promoter, a uidA sequence and a second sequence of interest (an aphA6 coding region lacking a 3' sequence), wherein the first sequence of interest is homologous to at least a portion of said second sequence of interest and assembled upon integration as a continuous sequence that can be expressed (pg 19, ¶2, to pg 20, ¶1; pg 41, ¶2, to pg 43, ¶3; Fig. 20-22). Herz et al disclose selecting transformants with the two sequences of interest as a continuous sequence because aph6 is a selectable marker (pg 19, ¶3; pg 42, ¶5). Additionally the first fragment of aphA6 is The rbcL 3' sequence would be an additional sequence of interest on the first DNA construct, and the promoter and uidA sequence would be additional sequences of interest on the second DNA

construct. An additional DNA molecule was introduced with the first DNA molecule; the additional DNA molecule encoded aadA, a sequence of interest conferring resistance to spectinomycin and streptomycin aadA (19, ¶2; pg 41, ¶2); the additional DNA molecule would contain sequence segments homologous the said first a second sequences of interest, wherein the sequence segments are at least two nucleotides long.. The first and second regions homologous to the plastid genome correspond to a continuous sequence of the tobacco plastid genome. The first and second DNA constructs would be a kit-of parts.

Applicant urges that claim 1 has been amended to recite that the first DNA construct comprising only one region homologous to the plastid genome, which was previously indicated as allowable (response pg 22).

This is not found persuasive because the indication was incorrect. There is no requirement in the claims that the second sequence is introduced after the first; thus, either sequence can the first and either the second. In Herz et al, the first DNA construct is the one comprising a second region homologous to the plastid genome (rpl32/sprA), a promoter, a uidA sequence and a second sequence of interest (an aphA6 coding region lacking a 3' sequence).

***Claim Rejections - 35 USC § 103***

7. Claims 1, 3-9, 12-15, 18-20 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herz et al (WO 02/055651). Due to applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 27 September 2007, as applied to claims 1, 3-9, 12-15, 18-20 and 23-24. Applicant's arguments filed 16 January 2008 have been fully considered but they are not persuasive.

The claims are drawn to a method of tobacco plastid transformation comprising introducing separately into plastids two DNA constructs, wherein the first construct comprises a first sequence of interest containing a 5' part of a gene of interest and the second construct comprises a second sequence of interest comprising the 3' part of the gene of interest. The claims are also drawn to the method wherein the first or second construct comprises a selectable marker gene outside the sequence of interest and a region homologous to a plastome region.

The teachings of Herz et al are discussed above. Herz et al do not disclose the first construct comprising the 5' part of a gene of interest and the second construct comprising the 3' part of the gene of interest or seeds produced from the plants.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of plastid transformation as taught by Herz et al, to change the order in which the portions of the gene of interest is introduced into the plastid or include the selectable marker for the first transformation on the first DNA construct. One of ordinary skill in the art would have been motivated to do the first because selection of having the 5' part of a gene of interest on the first DNA construct or the 3' part of the gene of interest on the first DNA construct is an obvious design choice. One of ordinary skill in the art would have been motivated to do the second because Herz et al teaches such an arrangement of selectable marker on the DNA construct in Fig. 12; using this over co-transformation with a second construct is an obvious design choice. One of ordinary skill in the art would have been motivated to produce seeds from the plants as this is how plants are propagated; they would also be produced in the course of the plant growing.

Applicant urges that claim 1 has been amended to recite that the first DNA construct comprising only one region homologous to the plastid genome, which was previously indicated as allowable (response pg 23).

This is not found persuasive because the indication was incorrect. There is no requirement in the claims that the second sequence is introduced after the first; thus, either sequence can be the first and either the second. In Herz et al, the first DNA construct is the one comprising a second region homologous to the plastid genome (rpl32/sprA), a promoter, a uidA sequence and a second sequence of interest (an aphA6 coding region lacking a 3' sequence).

8. Claims 1, 3-10, 12-15, 18-20 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herz et al (WO 02/055651) in view of Maliga et al (1995, US Patent 5,451,513). The rejection is repeated for the reasons of record as set forth in the Office action mailed 27 September 2007, as applied to claims 1, 3-10, 12-15, 18-20 and 23-24. Applicant's arguments filed 16 January 2008 have been fully considered but they are not persuasive.

The claims are drawn to a method of tobacco plastid transformation comprising introducing separately into plastids two DNA constructs, each comprising only a part of a gene of interest, wherein expression of the gene of interest involves trans-splicing.

The teachings of Herz et al are discussed above. Herz et al do not disclose the expression of the gene of interest including RNA trans-splicing.

Maliga et al teaches plastid DNA constructs in which expression of the gene of interest involves trans-splicing (column 19, line 59, to column 20, line 49).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of plastid transformation as taught by Herz et al, to have

expression of the gene of interest involve trans-splicing as described in Maliga et al. One of ordinary skill in the art would have been motivated to do so because Maliga et al teaches that the trans-splicing system facilitates recovery of plastid transformants (column 20, lines 32-35).

Applicant urges that claim 1 has been amended to recite that the first DNA construct comprising only one region homologous to the plastid genome, which was previously indicated as allowable (response pg 23).

This is not found persuasive because the indication was incorrect. There is no requirement in the claims that the second sequence is introduced after the first; thus, either sequence can be the first and either the second. In Herz et al, the first DNA construct is the one comprising a second region homologous to the plastid genome (rp132/sprA), a promoter, a uidA sequence and a second sequence of interest (an aphA6 coding region lacking a 3' sequence).

9. Claims 17 and 27 are free of the prior art, given the failure of the prior art to teach or suggest a method of tobacco plastid transformation comprising introducing separately into plastids two DNA constructs, the each construct comprising only one region homologous to the plastid genome, wherein the first sequence of interest is homologous to at least a portion of said second sequence of interest and assembled upon integration as a continuous sequence that can be expressed. Claim 2 is free of the prior art, given the failure of the prior art to teach or suggest a method of tobacco plastid transformation comprising introducing separately into plastids two DNA constructs, the first DNA construct comprising a first region homologous to the plastid genome and a first sequence of interest and the second DNA construct comprising a second region homologous to the plastid genome, a promoter, a uidA sequence and a second sequence of



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interest, wherein DNA constructs are introduced by co-transformation. Claim 11 is free of the prior art, given the failure of the prior art to teach or suggest transforming plastids with two DNA constructs, wherein the constructs each comprise a portion of a sequence of interest and homologous regions outside the sequence of interests, wherein the homologous regions allow excision of the sequence of interest.

### *Claim Objections*

10. Claims 2, 11 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Claim 27 is allowed.

### *Conclusion*

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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Anne Kubelik, Ph.D.

July 2, 2008

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638